

REMARKS

The Office Action of June 15, 2007, presents the examination of claims 14-18, 20-24 and 32-41. Claims 14-18, 20-24, 32, 36, 38, 39 and 41 are canceled herein. Claims 33-35, 37 and 40 are amended. Claim 42 is added. Claims 33-35, 37, 40 and 42 are pending.

Withdrawn method claims 33 and 34 are amended so as to provide dependence upon a pending claim and to maintain their scope within that of presently examined composition claims, thus preserving Applicants' right to rejoinder of these claims to the instant application should the pending composition claims be found allowable.

In general, the amendments to the claims delete subject matter. Claim 37 is amended to recite that the luciferase is one from a firefly. Support for this term in the claims is plainly present throughout the instant specification. The amended sequence in claim 40 and in new claim 42 is a segment of the sequence from SEQ ID NOS: 4, 6 and 8.

Applicants reserve the right to file an application directed to the deleted subject matter pursuant to 35 USC § 120.

Specification and claim objections

Dependent claims 18 and 20-22 are objected to as reciting "a" native luciferase. The Examiner suggests that the article should be definite ("the"). Claims 18 and 20-22 are canceled, rendering this rejection moot.

The specification is objected to as erroneously identifying SEQ ID NOS: 1 and 2 as amino acid sequences at page 7. The specification is amended to correctly identify the relevant amino acid sequences, thus obviating this objection.

Claims 37-40 are objected to as failing to comply with the requirements of 37 CFR §§ 1.821-1.825. Applicants request that this objection be held in abeyance until claims 37 and 40

(and 42) are found allowable, at which time Applicants will file an amended Sequence Listing and further amendment to the claims so as to comply with these rules. A telephone call from the Examiner to indicate allowability of claim 37 and 40 (and 42) prior to issuance of a Notice of Allowance, so that Applicants may make these amendments by a supplement to this Amendment, would be appreciated.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 35 and 37-40 are rejected under 35 USC § 112, first paragraph, as allegedly presenting subject matter not described in the specification. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Examiner asserts that the present specification only describes isolation of mutant luciferases derived from HEIKE or GENJI fireflies using primers of SEQ ID NO: 1 or 2. That is, the Examiner asserts that the specification only describes obtaining mutant proteins from these two organisms and no others.

Applicants strongly disagree with this position of the Examiner, at least for the reasons explained previously. The isolation of mutant proteins from HEIKE or GENJI fireflies is described in the specification as working examples of the invention, but it is well-established law that the claims of a patent need not be limited to the scope of its working examples. *See, e.g. In re Robins*, 166 USPQ 552 (CCPA 1970). Nonetheless, to advance the prosecution of the present invention, claim 35 is amended to recite the source organisms deemed by the Examiner to be adequately described. Accordingly, the rejection based on this ground is overcome and should be withdrawn.

The Examiner further asserts that the amino acid sequence PXAVVVLX₄₉₀GKXMTE is not described in the specification. The Examiner objects to the inclusion of "any amino acid" as those which may be present at the positions X, other than 490, in the recited short sequence. The Examiner indicates that this is a new matter rejection.

Applicants strongly disagree with this assertion of the Examiner. Nonetheless, the claims are amended so as to advance the prosecution of the instant application. In claim 40, the short sequence specifically recites a segment of amino acids in which the variable residue is limited to position 490. The Examiner cannot reasonably assert that a skilled molecular biologist is unable to visualize the possible variant amino acids that might be placed at that position. The disclosure of the present application makes quite clear that the position 490 is a determinant of surfactant resistance and that enzymes having an amino acid other than glutamic acid at this position are resistant to surfactant. See, e.g. page 3, lines 8-11 of the specification.

The Examiner also objects that claim 35 is limited only by its function, no structure of the claimed protein is recited. The Examiner has argued that the structure of an enzyme that would be operable in the present invention is unpredictable. The Examiner thus suggests that the structure encompassed by the invention is not amenable to precise description. In such a circumstance, the Court of Appeals for the Federal Circuit has approved the use of product-by-process language to describe an invention, at least in instances such as the present application, in which the process steps recited in the claims have actually been used to obtain an embodiment of the invention; that is, the process has been reduced to practice prior to filing of the application. See, e.g. *Fiers v. Revel*, 25 USPQ2d 1601, 1605. Applicants submit that the product-by-process language of claim 35 is appropriate and adequate and the scope of the claim is well-described in the present specification. Furthermore, in some instances, i.e. when supported by a deposit of a microorganism embodying the invention or by disclosure of sufficient information to allow practice of the invention without recourse to a deposit, describing an invention by its function alone is sufficient that claims relying upon such support cannot be rejected as a matter of law. To sustain a rejection on such facts, the Examiner must make a detailed examination of the facts surrounding the claims and explain why such facts lead to a conclusion that the written description of the invention is inadequate. *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 63 USPQ2d 1609, 1612-13 (Fed. Cir. 2002).

As explained previously, the present specification includes disclosure of firefly luciferase nucleotide sequences that can serve as templates for producing the luciferases of the instant

invention. The specification also discloses amplification primers, SEQ ID NOS: 1 and 2, that are useful for amplifying polynucleotides obtained from various organisms, including fireflies, for use in the present invention. Furthermore, the specification discloses that bacteria harboring DNA representing cloned luciferase proteins can be exposed to chemical or radiation mutagens so as to randomly modify the luciferase genes and produce mutant proteins for activity screening. Alternatively, the specification discloses that specifically desired mutations can be introduced by genetic engineering methods known in the art. Furthermore, the techniques and polynucleotides so described were used to produce mutant luciferases according to the claims (Examples 2 and 3).

There is simply no way that the facts of the present application sustain an allegation that the inventors of the present invention did not “possess” an invention of scope described by the present claim 35.

In claim 37, the short sequence recited remains variable at two positions other than position 490, however, the mutant enzyme is recited as one that is a firefly luciferase. The two additional positions that are variable in claim 37 are those that demonstrate variation among the species disclosed in the instant sequence listing. The instant specification also makes very clear that firefly luciferases may be used as starting points for producing mutant enzymes of the invention. Furthermore, a number of “firefly luciferases” were known in the art at the time the present invention was made. To provide their detailed structure adds nothing to the present disclosure, and so such detailed description of these species is not required to support a claim of similar scope. *Capon v. Eshhar*, 67 USPQ2d 1078 (Fed. Cir. 2005). Applicants submit that the specification provides ample evidence that the inventors “possessed” at the time of filing of the instant application, the invention presently described by claim 37. Accordingly, the instant rejection should be withdrawn as to this claim.

Claims 14-18, 20-24, 32 and 35-41 are also rejected under 35 USC § 112, first paragraph for alleged lack of enablement by the specification. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Claims 14-18, 20-24, 32, 36, 38, 39 and 41 are canceled, rendering the rejection moot as to those claims. Applicants have previously presented a detailed analysis of the enablement of the claims according to the factors set forth in *In re Wands*.

In relation to claim 35, the Examiner admits that the specification enables a mutant luciferase that is the SEQ ID NO: 4 or 6 having a mutation at position 490. The Examiner cannot reasonably maintain a position that one of ordinary skill in the art who is enabled to make and use a mutant firefly luciferase of these two embodiments is not also enabled by the instant specification to make another mutant luciferase having a particular activity starting from knowledge in the art and provided by the specification of how to amplify DNA from a firefly producing an luciferase using the primers of SEQ ID NO: 1 and 2 disclosed in the specification, and then proceeding to express the DNA, perhaps after optionally mutating it by random or by site-directed methods (both are considered known in the art), and test the expressed protein for activity in the presence of a surfactant. It may not be predictable in advance of this experimentation what the exact amino acid sequence of the resulting luciferase will be, but it is predictable that a luciferase retaining 85% of wild-type activity in the presence of a surfactant can be produced by experimentation that is expected by one of ordinary skill in the art and well guided by the present specification. That is all that is required by the statute. See, *In re Wands*, 8 USPQ2d 1400, 1406-07 (Fed. Cir. 1988).

Claim 37 recites a firefly luciferase having at least short portion of its sequence defined. Again, the Examiner should note that the scope of this claim is well within the scope of the amount of variation easily made and tested by the skilled artisan using the disclosure of the instant specification and his knowledge of the art.

The Examiner seems to be interpreting the claims a bit too broadly as well. Applicants note the Examiner seems to believe the claims require only that the short sequence PXAVVVLX₄₉₀GKXMTE must be present in the protein claimed. However, this overlooks the recitation in claim 35 that the encoding nucleic acid must include the nucleotides of SEQ ID NO: 1 and SEQ ID NO: 2, or their complements, which are incorporated from the primers during the amplification process. The encoding polynucleotide would be the entire sequence of the

template polynucleotide, obtained from a firefly, lying between the hybridization sites of these two primers. Thus, the protein of claim 35 is of a defined length. In claim 37, the protein is recited as a firefly luciferase. Such a short sequence of only 14 amino acids would not be considered a "firefly luciferase" by one of ordinary skill in the art. In both claims, the level of activity required of the protein is stated; non-functional embodiments are excluded.

Rejection over prior art

Claims 14-18, 20-24, 32 and 35-41 are rejected under 35 USC § 102(e) as anticipated by Hirokawa '859. Claims 14-18, 20-24, 32, 36, 38, 39 and 41 are canceled, rendering this rejection moot as to those claims. The rejection is respectfully traversed with respect to claims 35, 37 and 40. Reconsideration and withdrawal thereof are requested.

Applicants have previously explained that the Hirokawa '859 reference is silent about the resistance of the luciferases disclosed in the reference to surfactant. To those reasons for lack of anticipation, Applicants now clarify, by the attached Declaration of Mr. Murakami, that the firefly luciferase having a mutation at position 490 disclosed in the '859 application, but not claimed, was conceived and reduced to practice, and thus invented, by him among the co-inventors listed on the '859 patent. Accordingly, the subject matter disclosed in the '859 application that is asserted by the Examiner to anticipate the presently claimed invention is not the invention "of another" and so the present rejection must be withdrawn.

The attached Declaration of Mr. Murakami also makes clear that the various buffers described in the '859 patent in its Example 5 (testing for activity in the presence of buffers of various pH) are not "surfactants", confirming that the '859 patent is silent as to this property of the instantly claimed proteins. This evidence supports Applicants' assertion that the '859 patent does not anticipate the presently claimed invention, either expressly or inherently.

CONCLUSION

In view of the above amendments and arguments, Applicants believe the pending application is in condition for allowance.

Application No. 10/829,250
Amendment dated December 13, 2007
Reply to Final Office Action dated June 15, 2007

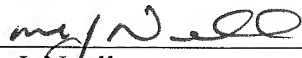
Docket No.: 1254-0281PUS1

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell Reg. No. 36,623 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: December 13, 2007

Respectfully submitted,

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Attachments: Declaration of Seiji Murakami